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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
YU, MISOOK	
ART UNIT	PAPER NUMBER
1642	7

DATE MAILED: 06/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No. 09/865,879	Applicant(s) RONINSON ET AL.	
	Examiner Misook Yu	Art Unit 1642	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-7,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election of group II with species beta-IG-H3, claims 8-18 in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-7, 19, and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

Claims 8-18 are examined on merits.

Specification

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. The claims define the invention by stating that "the promoter does not contain a RARE site." Therefore understanding of the meaning of "a RARE site" is essential to practice the invention. The only definition of RARE in the specification is reference to a publication (the paragraph bridging page 11 and 12 and page 13 lines 17-21). Therefore, information essential to practice the invention is incorporated by reference. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 26 line 22, for example. Applicant is

required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the following informalities: The specification contains blank lines at numerous places for example, page 28, 2nd paragraph, and page 12. fixed

Appropriate correction is required.

Claim 8-11 are objected to because it depends on a nonelected claim. Appropriate correction is required. fixed

For the purpose of this office action, however, the limitations of claim 7 will be included in the examination of claims 8-11.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

and 17 mr 2-14-03
Claims 13 ~~is~~ are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 is unclear because they refer to NCBI accession numbers rather than to sequences set forth in the specification. This is seen as an improper incorporation by reference, since the information required to describe and enable the required sequences is found in the NCBI database, extraneous to the application. Furthermore, since NCBI sequences are not irrevocably fixed but are corrected and updated as additional sequence information becomes available, the NCBI accession numbers may refer to sequences which change after the application filing date. For example, when Genbank Accession No. M35878.1 in line 2 of claim 13 is searched online in the NCBI database, Genbank Accession No. M35878 is the result. The information under Genbank Accession No. M35878 states Genbank Accession No. M35878.1 (GI:184522) fixed

is was replaced by gi:763445 on 04 April 2002, after the filing date of this application. Further the examiner was unable to locate Genbank Accession No. M35878.1 recited in claim 13. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). Furthermore, if a required sequence was not set forth in the specification as filed, and was not publicly available from Genbank at the time the application was filed, the amendment will be treated as an attempt to introduce new matter (similar to attempts to incorporate essential material by reference to unpublished material). In addition, note that the amendment will probably require a replacement Sequence Listing, to add the sequences which are added to the disclosure.

Claim 13 refers to itself and therefore it is indefinite. pro-ed

For the purpose of this office action, the examiner will assume that claim 13 refers to claim 12. However, this treatment does not relieve applicant the burden of responding to this rejection.

Claim 17 recites "assaying for an activity of the cellular gene product" but it is not clear what the metes and bounds are for "assaying for an activity of the cellular gene product". Does the "assay for an activity of the cellular gene product" mean a specific activity for each of the 12 cellular gene product disclosed in claim 13, for example, enzymatic activity assay for the retinal oxidase? Or does "assaying for an activity of the cellular gene product" mean something else? The specification does not define what is mean by "assaying for an activity of the cellular gene product. drop

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-16, and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for MCF-7 cells, does not reasonably provide enablement for any mammalian cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Claims 8-16 and 18 are drawn to method of identifying compounds that induce expression of a retinoid-inducible gene by an assay involving the use of either a mammalian cell (claims 12-18) or a mammalian cell which contain a recombinant expression construct encoding a reporter gene operably linked to a retinoid-inducible promoter from a gene whose expression is inducded by a retinoid, wherein the retinoid-inducible promoter does not contain a RARE site. The specification teaches in Figure 2 and 3 that all the cellular genes listed in claim 13 are induced in response to treatment of retinoic acid in MCF-7 breast carcinoma cell line but does not teach the detection of the retinoid-inducible gene expressions could be possible in any other mammalian cell. Cohick et al (1998, Journal of Endocrinology 157: 327-336) teach at abstract, in Figure 2 and Figure 3B top panel that IGFBP-3 recited in the instant claim 13 is not induced in response to retinoic acid treatment in another mammalian cell, namely MAC-T epithelial cell line. Considering the broad scope of the claims, the limited teachings of the specification and lack of examples, it is concluded that undue experimentation would be required to enable the full scope of the claims.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 17 is drawn to identifying compounds by ***an assay capable of detecting an activity of retinoid-inducible cellular gene product*** that does not contain RARE sites. The specification fails to describe an assay capable of detecting an activity of retinoid-inducible genes that do not

contain RARE sites. What is the control? How do you measure? What are the reagents and active method steps that constitute the assay recited in claim 17? It is concluded that applicant does not adequately describe the instantly claimed invention.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 17 is drawn to identifying compounds by ***an assay capable of detecting an activity of retinoid-inducible cellular gene product*** that does not contain RARE sites. The specification does teach any assay capable of detecting an activity of retinoid-inducible cellular gene product that does not contain RARE sites. The specification, however, teaches an assay using reporter construct at page 31 lines 16-page 32 line3. Considering the broad scope of the claims, the limited teachings of the specification and lack of examples, it is concluded that undue experimentation would be required to enable the full scope of the claims.

dmf.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 8-16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adamo et al (1992, Endocrinology 131:1858-1866), Miller (1998, Cancer 83: 1471-82), Han et al (1997, J. Biol. Chem. 272: 13711-13716), and US Pat. 5,795,726 (18 Aug.1998).

Claims 8-16 and 18 are drawn to method of identifying compounds that induce expression of a retinoid-inducible gene by an assay involving the use of either a mammalian cell (claims 12-18) or a mammalian cell which contain a recombinant expression construct encoding a reporter gene operably linked to a retinoid-inducible promoter from a gene whose expression is inducded by a retinoid, wherein the retinoid-inducible promoter does not contain a RARE site, wherein the assay utilizes detection method known in the art (as recited in instant claims 9-11, 16, and 18), wherein the retinoid-inducible cellular gene inhibits growth of the cell (as recited in claim 14).

Adamo et al (1992, Endocrinology 131:1858-1866) teach retinoid-induced growth inhibition (recited in instant claim 14) of MCF-7 breast carcinoma cell line is associated with IGFBP-3 expression (one of the cellular genes recited in instant claims 4, 6, 13 and 15), wherein the retinoid-induced expression is detected using the conventional detection method recited in the instant claims 12, 16 and 18: Note abstract, Materials and Methods section at page 1859, 1st paragraph of the left column at page 1859 and page 1861, Fig. 4A, line 8 of page 1862 to 1st paragraph, left column, page 1863, and the paragraph bridging page 1863 and 1864. Han et al (1997, J. Biol. Chem. 272: 13711-13716) also teach in Figure1 that IGFBP-3 is induced by retinoid: Note also Experimental Procedures at page 13711-2. Although both Adamo et al (1992, Endocrinology 131:1858-1866) and Han et al (1997, J. Biol. Chem. 272: 13711-13716) are silent about the nature of the promoter, i.e. the presence or absence of the RARE site (recited in instant claim 12 b), the prior art teaches that IGFBP-3 is inducible by retinoid and this property is the inherent nature of IGFBP-3 promoter. Thus, both Adamo et al (1992, Endocrinology 131:1858-1866) and Han et al (1997, J. Biol. Chem. 272: 13711-13716) teach the active method steps recited in the instant claims 12-16, and 18, and the fact that IGFBP-3 inherently possesses promoter that could be induced by retinoid. Neither Adamo et al nor Han et al teach the purpose stated in the preamble of the instant claim 12, i.e. the need to identify other compounds that could induce the retinoid-inducible cellular genes. However, Miller (1998, Cancer 83: 1471-82) teaches at page 1472, left column, 1st paragraph and left column, 3rd paragraph, right column of page 1472 to 2nd paragraph left column, page 1473 that retinoids and its

maintain

analogs are useful in treatment of cancer and biological effects of retinoids are modulated through the activated nuclear receptors including multiple nuclear steroid hormone receptor family members, wherein the activated nuclear receptors control the expression of genes that mediate retinoid effects including apoptosis. Miller further teaches, in the left column, page 1473, the last 5 lines of 2nd paragraph, the need for more research to develop alternative a novel retinoid coumpound to which resistance is not so easily developed and that lacks the toxicity and other side-effects of retinoids in current clinical use: Also note right column, page 1475 to end of page 1467. Miller does not teach the specific method recited in instant claim 8-11. However, US Pat. 5,795,726 (18 Aug.1998) teaches in column 66, lines 8-29 an assay that detects transcriptional activating properties by use of a cell which contain a promotor linked to an operative reporter gene.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine teachings of all of the above references to identify a compound that might have potential anti-cancer effect.

Conclusion

No claim is allowed. However, applicant is informed that this examiner's search did not uncover any prior art that teaches beta-IG-H3 (the elected species) is inducible by retinoids. If the claims are amended to exclude the generic claims and species that were known to be induced by retinoids before the effective filing date of the instant application, the method for identifying compounds with beta-IG-H3 (the elected species) are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Misook Yu whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-

305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu Ph.D.
June 12, 2002

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